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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/142,613	04/19/99	ISHIGURO K	1416/OP551PC

HM12/1025

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EXAMINER	
TURNER,S	
ART UNIT	**PAPER NUMBER**
1647	13

DATE MAILED: 10/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/142,613	Ishiguro
Examiner	**Group Art Unit**
Sharon L. Turner, Ph.D.	1647

☒ Responsive to communication(s) filed on *7-19-00, 8-22-00*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-7* is/are pending in the applicat

Of the above, claim(s) *the nonelected species* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4* is/are rejected.

☒ Claim(s) *5-7* is/are objected to.

☒ Claims *1-7* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *12*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Art Unit of U.S. Patent application SN 09/142,613 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Examiner Turner, Technology Center 1600, Art Unit 1647.

Election/Restriction

2. Applicant's election of Group I, claims 1-6, species at phosphorylation site 199 and SEQ ID NO:2 in Paper No. 11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. The examiner notes that the original restriction was set forth under 35 USC 121, US restriction practice instead of 35 USC 372 for applications filed under 35 USC 371. The examiner notes that the group accordingly includes claim 7. The species election remains as previously set forth. The claims should be amended to the elected species.

Claim Objections

4. Claims 5-7 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not serve as the basis for another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

5. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 fails to further limit the antibody recognizing the phosphorylation sites of phosphorylated tau protein which sites are one or more amino acid residues selected from serine at position 199 of an amino acid sequence of SEQ ID NO:1. Such recitations have already been recited in claim 2. Thus, claim 3 fails to further limit claim 2.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification discloses an antibody obtained by using as an immunogen a partial peptide comprising phosphorylation sites of phosphorylated tau protein in a paired helical filament. Claims 2 and 3 are drawn to such sequences of SEQ ID NO: 1 which correspond to partial peptide sequences of tau. This SEQ ID NO provides written description for those partial

peptide species. However, claims 1 and 4 to the extent of claim 1, directed to partial peptide sequences of tau which lack defined residues, encompass sequences which lack written description support under 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is for purposes of the 'written description' inquiry, whatever is now claimed." (See Vas-Cath at page 1116.)

With the exception of the partial peptides defined from SEQ ID NO:1 of the instant application, the skilled artisan cannot envision the detailed chemical structure of the encompassed amino acids and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The specific nucleic and amino acids are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only partial peptides of SEQ ID NO:1, but not the full breadth of claims meet the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

8. Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies reactive to those peptides defined by SEQ ID NO:1, does not reasonably provide enablement for antibodies generated to undisclosed peptide sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation. The factors relevant to this discussion include the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims.

Claims 1 and 4 recite antibodies obtained by using as an immunogen a partial peptide comprising phosphorylation sites of phosphorylated tau protein in a paired helical filament. However, the skilled artisan recognizes the unpredictability in the art associated with the prediction of peptide function based upon divergent structure, see in particular Skolnick et al.,

Trends in Biotech 18(1):34-39, 2000, abstract and Box 2. In addition, the skilled artisan recognizes the unpredictability in the art with respect to the prediction of immunogenicity with respect to alterations of single amino acid residues, see in particular Choh et al., PNAS., 77(6):1312-24, 1980. Thus, for those divergent peptide structures which lack written description support, the skilled artisan would be required to perform further undue experimentation to discover those peptides which possess the properties of stimulating antibodies reactive with phosphorylation sites of phosphorylated tau protein and which are useful for the detection of Alzheimer's disease.

Thus, for these reasons it would take further undue experimentation on behalf of the skilled artisan to make and to use the claimed invention.

Priority

9. Acknowledgment is made of applicant's claim for foreign priority based on application PCT/JP97/00804 filed 3/13/97 and application 8-56090 filed in Japan on 3-13-96. It is noted, however, that applicant has not filed a certified copy of the Japanese application as required by 35 U.S.C. 119(b) or English translations of the priority documents as required and therefor the effective filing date awarded claims 1-7 is the US filing date of 4-19-99. Art is applied accordingly.

Claim Rejections - 35 USC § 102 or 103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by IDS Reference Vandermeeren et al., J. of Neurochemistry 61:1828-34, 1993.

Vandermeeren teach detection of tau proteins in normal and Alzheimer's Disease CSF with a sensitive sandwich ELISA, see in particular title. The sandwich assay utilizes monoclonal antibody AT8 which recognizes abnormally phosphorylated serines 199-202 in tau. The antibody recognizes partial peptide sequences of SEQ ID NO:1. Thus the reference teachings anticipate the claimed invention.

12. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by IDS Reference Kimura et al., Dementia, 7:177-81, 1996.

Kimura et al., teach sequential changes of tau site specific phosphorylation during development of paired helical filaments, see in particular title. Kimura et al., teach generation of polyclonal antibody Anti-PP1 in particular which recognizes phosphoserine 199 and 202, see in particular Materials and Methods, p. 178, column 1, lines 23-25. In addition, Kimura teach analysis of immunoreactivity in Nondemented and Alzheimer's Disease Brains, see in particular

pp. 178, column 2-p. 180, column 1 and Table 1. Tau comprises partial peptide sequences of SEQ ID NO:1. Thus, the reference teachings anticipate the claimed invention.

13. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by IDS Reference Yamaguchi et al., Acta Neuropathol., 92:232-241, 1996 and Takahashi et al., J of Neurochemistry, 64:1759-68.

Yamaguchi et al., teach antiserum PS199 directed to the phosphorylated synthetic peptide of tau 195-205 which recognizes phosphorylated Ser199 of tau and the detection of neurofibrillary tangles in control, Alzheimers Disease and Down Syndrome brains, see in particular p. 233, column 1, lines 37-39 and Figures 2-6. Thus the reference teachings anticipate the claimed invention.

Takahashi et al., also teach antiserum PS199 antibodies directed to phosphorylated Serine199 and analysis of immunoreactivity in rat brain, see in particular title, abstract.

14. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Biernat et al., EMBO J., 11(4):1593-97, 1992.

Biernat et al., teach that the switch of tau protein to an Alzheimer-like state includes the phosphorylation of two serine-proline motifs upstream of the microtubule binding region using monoclonal antibody AT8 which recognizes the phosphorylation of serines 199 and/or 202, see in particular title, abstract. Biernat includes analysis of AD brain, see in particular Figure 7. Thus, the reference teachings anticipate the claimed invention.

Status of Claims

15. No claims are allowed.

16. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
October 23, 2000

CHRISTINE SAOUD
PATENT EXAMINER
Christine Saoud